REMARKS

After entry of this amendment, claims 177, 196 and 198 are pending and under consideration. Claim 177 has been amended to delete the words "binds to". Claim 197 has been canceled to expedite prosecution. Applicant uses the paragraph numbering of the final office action in responding to the Examiner's comments.

¶3. Priority

The Examiner denies priority to US Application No. 60/067,740 filed December 2, 1997 because the specification allegedly lacks supports for administration of 10D5 antibody. In reply, for purposes of responding to this office action, the Applicant will accept the Examiner's determination of priority. Applicant reserves the right to show an earlier date of invention should it become relevant.

¶4. Information Disclosure Statement

The Examiner crossed off cite nos. 631, 632 and 696 on the PTO/SB/08A form submitted with the supplemental IDS filed August 18, 2006. The references were not considered because they were allegedly not received. For the Examiner's convenience, Applicant resubmits cite nos. 631, 632 and 696.

Applicant respectfully points out that the supplemental IDS states that cite nos. 631 and 632 can be found in US Application No. 09/322,289, filed May 28, 1999. (*See* page 1 of the supplemental IDS, attached hereto as Exhibit A). Thus, cite nos. 631 and 632 should have been considered. Cite no. 696 was submitted with the supplemental IDS as evidenced by date stamped postcard submitted herewith as Exhibit B. Thus, cite no. 696 should have been considered.

Cite no. 639 filed August 18, 2006 was not considered by the Examiner because the citation did not include a date. The reference was cited as reference X by Examiner Johnalyn Lyles in related case, US Application number 10/923,471, as evidenced by page 1 of the PTO-892 form attached to the final office action mailed August 24, 2005 for Application number

10/923,471, attached hereto as Exhibit C. The Examiner of the instant case may wish to ask Examiner Lyles what the publication date of the reference she cited as reference X is.

¶5. As suggested by the Examiner, claim 177 has been amended to correct a typographical error. The words "binds to" have been deleted. Accordingly, the objection is moot.

¶6. The Examiner has rejected claims 177 and 196-198 under 35 U.S.C. §112, first paragraph as allegedly containing subject matter which is not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner has indicated that the requirement of 35 U.S.C. §112 may be satisfied by filing of an affidavit or declaration by applicants, assignees or a statement by an attorney of record and amendment of the specification.

Applicant respectfully points out that a declaration by an agent of record was duly submitted to the Patent Office at the time of filing the instant application. This declaration can be found in USPTO PAIR website under "Transmittal of New Application" dated April 19, 2004. For the Examiner's convenience, Applicant resubmits herewith the declaration as Exhibit D. The declaration states "The deposit was made pursuant to the provisions of the Budapest Treaty. A copy of the ATCC receipt is attached as Exhibit 1." and "All restrictions, on the availability to the public of the cell line identified in paragraph 1 above will be irrevocably removed upon the issuance of a patent from the above-captioned application."

Applicant has amended paragraph [0266] of the specification published as US 2004 0219146 to recite the complete name and address of the depository. This amendment does not add new matter (*see In re Lundak*, 773 F.2d 1216, 227 USPQ 90 (Fed. Cir. 1985) and MPEP § 2406.01).

Applicant respectfully requests that this rejection be withdrawn.

¶7. The Examiner has rejected claim 197 under 35 U.S.C. §112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant has canceled claim 197. Cancellation of claim 197 should not be construed as an acquiescence in any ground of rejection.

In light of the cancellation of claim 197, this rejection is moot.

¶8. The Examiner has rejected claims 177, 196 and 198 under 35 U.S.C. §103(a) as allegedly being unpatentable over Becker (EP 0613007) in view of Hanan (1996. Amyloid:Int J. Exp. Clin. Invest. 3:130-133).

Becker is alleged to teach administration of antibodies raised against beta-amyloid for treatment of Alzheimer's disease and disclose routes of administration. The Examiner acknowledges that Becker does not teach antibody 10D5. Hanan is alleged to teach antibody 10D5. The Examiner acknowledges that Hanan does not teach methods of treating patients by administering antibodies. The Examiner alleges it would have been obvious to use 10D5 antibodies as taught by Hanan in the method of Becker. The Examiner alleges that the motivation would be to treat Alzheimer's disease, as taught by Becker and the Hanan disclosure that 10D5 antibodies are particularly effective in disrupting aggregates of A-beta, the mechanism underlying Alzheimer's disease. The rejection is respectfully traversed.

"To establish a prima facie case of obviousness based on a combination of the content of various references, there must be some teaching, suggestion or motivation in the prior art to make the *specific* combination that was made by the applicant." *In re Dance*, 160 F.3d 1339, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998) (emphasis supplied). The motivation must have sufficient "force" to "impel persons skilled in the art to do what applicant has done." *Ex parte Levengood,* 28 USPQ2d 1300, 1302 (BPAI 1993). There must also have been a reasonable expectation of success. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). Exploration of a "new technology or general approach that seemed to be a promising field of experimentation" does not provide a reasonable expectation of success. *In re O'Farrell*, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

Here, the asserted motivation of providing a compound to treat Alzheimer's disease would not have impelled one to the specific combination recited in the present claims. The proposed motivation is so general that it could be asserted as a basis for almost any research in the Alzheimer's field. The motivation would not have impelled one to any specific strategy rather than pursuing research in general.

Further, the cited art did not provide a reasonable expectation of success. There are several objective indications that both references evidence an immature field of research far removed from a therapeutic product. Neither reference provides any *in vivo* data showing an activity of any agent on Alzheimer's disease. Becker is an entirely prophetic application. Moreover, this application has been abandoned in all jurisdictions suggesting that even the owners of the Becker application were not feeling optimistic of success (IMPADOC printout attached hereto as Exhibit E). Hanan is based on *in vitro* aggregation experiments. The artisan looking at these studies would at most see possibilities for further research. It seems implausible that the artisan would have been impelled to produce 10D5 antibody to use as a therapeutic without any such further research.

The immature state of the art discussed in the cited references is also evident from the excerpt from a review article looking back at how the present inventor's contributions to immunotherapy of Alzheimer's disease changed the nature of the field.

> While the amyloid hypothesis has offered drug researchers a number of obvious targets and strategies, it also led to *the most surprising attempt to thwart AD.* In the late 1990's, long after his colleagues at Elan had tested their most promising compounds, Schenk suggested injecting a few mice with β amyloid itself. His goal was to raise an antibody or other immune response against plaques. "No one thought it would work. Even after the experiment was done, the results weren't analyzed for a while," recalls Schenk.
>
> The results were stunning. The immunization slowed or prevented the development of β-amyloid plaques in young mice and even wiped away preexisting ones in older mice. *The episode illustrates how one person's idea can change the direction of a company or a field.* "Dale was really brave," says John Trojanowski of the University of Pennsylvania School of Medicine in Philadelphia.

> *How does big pharma react when a disease-treating strategy such as the Elan vaccine comes out of the blue?*
>
> Science, 309, 731-734 (2005) (emphasis supplied) (Exhibit F).

Although these comments were made primarily with reference to active immunotherapy rather than passive immunotherapy as claimed, they illustrate more generally that the first demonstration of modification of disease modification in an animal model by an immunotherapeutic approach was regarded as a dramatic and surprising news that changed the direction of the field. It follows that those in the field did not assume that Alzheimer's disease could be successfully treated with antibodies based on speculation from earlier *in vitro* experiments in the cited references.

Numerous similar comments have been made by disinterested third parties after learning of the first publication of the present inventor's results.

> This is the first time that anyone has stopped the development of amyloid plaques in a mouse model of Alzheimer's.... This is a major step forward. . .. If it does work, it would stand as one of the great scientific success stories of all time.
>
> Marcelle Morrison-Bogorad of the National Institute on Aging in Science News Online 156, 2 (July 10, 1999), Exhibit G.
>
> It's wild and amazing. . ..Almost all scientists would have dismissed the immunization approach. . . because of the dogma that the so-called blood-brain barrier keeps circulating antibodies out of the brain.
>
> Sangram S. Sisodia, University of Chicago in Science News Online 156, 2 (July 10, 1999), Exhibit G.
>
> Schenk surprised the Alzheimer's research community in June 1999 when he announced the vaccine worked to stop and even somewhat reverse the disease in mice. These mice were observed to perform better on memory tests.
>
> Detroit Free Press (July 23, 2001), Exhibit H.
>
> The idea was revolutionary because most Alzheimer's experts believe that the inflammation provoked by amyloid plaques contributes to destruction of brain cells. Many predicted that stirring up the immune system with a vaccine would only make the disease worse. . ..Schenk's 1999 paper on the Elan vaccine created

> a sensation not least because the unexpected findings suggested that vaccines might be helpful in disorders where no one had thought of using them. His results have since been confirmed by other researchers.
>
> Washington Post, May 8, 2001, Exhibit I.

The above comments show that disinterested observers were not convinced of immunotherapy as a viable treatment of Alzheimer's disease until publication of the first results showing disease modification in an animal model in present inventor's work in mid-1999. Absent a reasonable expectation of success of treating Alzheimer's disease, it was not obvious to combine the teachings of the cited references to arrive at the claimed invention.

For these reasons, Applicant respectfully requests that this rejection be withdrawn.

¶9. The Examiner has rejected claims 177, 196-198 under 35 U.S.C. §103(a) as allegedly being unpatentable over Becker in view of Hanan as applied to claims 177, 196 and 198 above, further in view of Miller (U.S. Patent 5,227,159).

Claims 177, 196 and 198 stand rejected as allegedly obvious over Becker in view of Hanan. Becker and Hanan are applied as above. Miller is alleged to teach repeated adminstration of the antibody as indicated by circulating antibody levels. The Examiner acknowledges that Miller does not teach antibody 10D5. This rejection is respectfully traversed for at least the reasons given above. Further, it would not have been obvious to combine Hanan with Miller. Moreover, as discussed above, claim 197 has been canceled. Thus, withdrawal of the rejection is respectfully requested.

¶10. Claims 177 and 196 are provisionally rejected for obviousness type double patenting as being unpatentable over claims 133-136 of copending US Application No. 10/232,030 in view of Queen (U.S. Patent No. 5,693,762). Claims 133-136 of copending Application No. 10/232,030 were canceled by the amendment filed April 13, 2006. Thus, the rejection is moot.

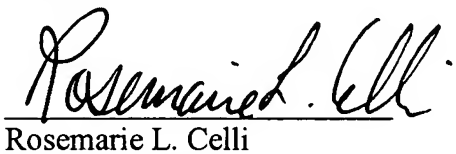
¶11. Claims 177 and 196 are provisionally rejected for obviousness type double patenting as being unpatentable over claims 18-20 of copending US Application No. 10/704,070 in view of Queen (U.S. Patent No. 5,693,762). Application No. 10/704,070 is now abandoned so the rejection is moot.

US Application No. 11/520,438 is a continuation of US Application No. 10/704,070. Should the claims of U.S. Application No. 11/520,438 be allowed before the present case, and the claims of the present application are allowed in their current form, applicant will provide a terminal disclaimer on notification of otherwise allowable subject matter.

CONCLUSION

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-625-8100.

Respectfully submitted,



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